DETAILED ACTION

Status of Application

1. The remarks, amendments and Declaration filed on 05/15/08 are acknowledged.

2. Claims 141-144 were added. Claims 2-5, 9, 37-38, 41, 43-45, 49-50, 106, 108, 110, 112-116, 121-122, 127-128 and 137-140 were amended.

3. Claims 10-35, 54-58, 60-105, 119-120, 123-126 and 129-136 were withdrawn.

4. Claims 1-9, 36-53, 106-118, 121-122, 127-128 and 137-144 are included in the prosecution.

Response to Arguments

Request for Interview

5. Applicant's request for an in-person interview is acknowledged. Applicant's representative called on 07/31/08 and suggested that an interview can be scheduled after the mailing of this office action. See attached Interview Summary.

Rejection of claims 1, 5-7, 36, 41-43, 45-47, 49, 122 and 127 under 35 USC § 102(b)

6. Applicant's arguments, see Page 31, filed 05/15/08, with respect to the rejection of claims 1, 5-7, 36, 41-43, 45-47, 49, 122 and 127 under 35 U.S.C. 102(b) as being anticipated by Nowak et al. (WO 01/03676) have been fully considered.

Applicant argues that for claim 1 to be anticipated, a prior art reference must teach a multi-compartment capsule as claimed, that includes a nutraceutical, a vitamin and/or a dietary supplement in both capsules. Nowak teaches liquid dextromethorphan in one chamber of the capsule and chlorpheniramine powder in the second chamber of the capsule (Page 10, Example 6). Applicant states that since these are not

nutraceuticals, vitamins or dietary supplements, claim 1 cannot be deemed anticipated by PCT '676. This was found persuasive and a rejection of claims 1, 5-7, 36, 41-43, 45-47, 49, 122 and 127 under 35 U.S.C. 103(a) as being unpatentable over Nowak et al. (WO 01/03676) follows.

Rejection of claims 2, 8-9, 38, 44, 48, 50-53, 106-118, 121, 128 and 137-140 under 35 USC § 103(a)

7. Applicant's arguments, see Page 33, filed 05/15/08, with respect to the rejection of claims 2, 8-9, 38, 44, 48, 50-53, 106-118, 121, 128 and 137-140 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nowak et al. (WO 01/03676) in view of Zimmer (US 5,310,555) have been fully considered but are not persuasive.

Applicant argues that Nowak does not suggest the "hard shell capsule" feature as recited in new claims 141 and 142. Applicant argues that the ordinary artisan would not have sought to apply the teachings of Nowak to a hard shell capsule according to the claims. Applicant argues that the artisan would have eschewed the unmodified teachings of Nowak.

This is not found persuasive because although Nowak does not expressly teach a "hard shell capsule", the supporting reference, Zimmer, suggests the use of a hard shell double capsule (capsule-in-capsule) to deliver mutually reactive or otherwise incompatible substances. While discussing the background prior art (in Col. 2, lines 45-56) Zimmer states that it is unlikely that Morishita's (US 4,695,466) soft outer capsules will be able to withstand common shipping, storage and administration conditions. Therefore, Zimmer suggests the use of hard shell gelatin capsules for the delivery of

mutually reactive or otherwise incompatible substances. One of ordinary skill in the art would combine this teaching of Zimmer with the capsule with at least two separate chambers, as suggested by Nowak, and produce the instant invention.

Response to the Declaration of Carey Bottom

8. Applicant submitted the Declaration of Carey Bottom on 05/15/08. Dr. Bottom states that in his opinion Nowak does not disclose or suggest that its teachings may be implemented in a hard shell capsule (Declaration, Page 2, point 9). Dr. Bottom states that the "pre-dried film" was critical to the septum concept of Nowak. Dr. Bottom states that it was common knowledge in the drug encapsulation community that capsules made from the pre-dried film, as developed by BioProgress, were not hard shell capsules but, in fact, were the antithesis of such capsules. Dr. Bottom also stated that the capsules made with the pre-dried film of Nowak had a tendency to fall apart within two months and would be unsuitable for human consumption because of the likelihood that incompatible drugs could come into contact with one another.

This is not found persuasive because the capsule with at least two separate chambers, as suggested by Nowak, is combined with the capsule with separate chambers in the form of a capsule-in-capsule, as suggested by Zimmer. Zimmer suggests the use of a hard shell double capsule (capsule-in-capsule) to deliver mutually reactive or otherwise incompatible substances. While discussing the background prior art (in Col. 2, lines 45-56) Zimmer states that it is unlikely that Morishita's (US 4,695,466) soft outer capsules will be able to withstand common shipping, storage and administration conditions. Therefore, Zimmer suggests the use of hard shell gelatin

capsules for the delivery of mutually reactive or otherwise incompatible substances. One of ordinary skill in the art would combine this teaching of Zimmer with the capsule with at least two separate chambers, as suggested by Nowak, and produce the instant invention.

Therefore, the rejection of 01/17/08 is maintained.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-2, 5-9, 36, 38, 41-53, 106-118, 121-122,127-128 and 137-144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nowak et al. (WO 01/03676) in view of Zimmer (US 5,310,555).

The claimed invention is a multi-compartment capsule comprising a first receiving chamber that comprises at least one ingredient having a first physical state and a second receiving chamber that comprises at least one ingredient having a second physical state. The first physical state of the ingredient in the first receiving chamber is different from the second physical state of the ingredient in the second receiving chamber and the ingredient in the first receiving chamber is different from the ingredient of the second receiving chamber.

Nowak teaches a capsule with at least two separate chambers. “The chambers of the capsule are completely discrete and separated from each other so that no communication between the chambers is possible. This means that the contents of the different chambers are kept separate from each other within the capsule until delivery. In most cases, different chambers of the capsule will contain different materials, possibly in different physical forms, e.g. liquid, solid (e.g. tablet, particulate, powdered), slurry etc., … The capsule is preferably internally divided by a dividing wall or septum, conveniently in the form of a median wall symmetrically arranged to form two chambers of similar size and shape. One or more chambers of the capsule may be further divided if required, e.g. by inclusion in a chamber of a smaller delivery capsule, constituting a further separate chamber” (Page 2). The capsule is used to deliver two separate pharmaceutical preparations (Page 3). The reference also discloses “the use of a pH sensitive coating on the material defining one chamber so that chamber contents are released at different delivery sites dependent upon pH” and the “use of enteric coatings such as cellulose acetate phthalate … to target release, e.g. within the stomach” (Page 4). Also disclosed is the “encapsulation of a wide range of pharmaceutical, culinary, cosmetic etc. ingredients, enabling delivery to different sites of different materials or delivery to the same site of materials that are desirably kept separate prior to delivery" (Page 6). Nowak also discloses “the encapsulation of both powders and liquids within discrete chambers in an ingestible capsule” (Page 7). Figure 1 shows that each chamber of the capsule “contains a metered amount of a different material … a

powdered or particulate material in chamber 18 and a liquid material in chamber 20 ..." (Page 8).

Nowak does not expressly teach a multi-compartment capsule further comprising a base and a corresponding cap where the cap is configured to provide a sealing relationship when engaging the base.

Zimmer teaches “a double capsule which includes live cultures of rumen bacteria in a first capsule which is enclosed with vitamin and mineral supplements in a second capsule” (Col. 3, lines 15-17). A capsule-in-capsule structure is shown (Figure 1). “The outer capsule outer capsule 24 has a top member 38 and a bottom member 40 in which top member 38 is locked to bottom member 40 with a groove 42 and a ridge 44” (Col. 5, lines 3-6). The capsule “preserves the activity of mutually reactive or otherwise incompatible substances by physically separating them during production, storage and administration. When live microorganisms are administered to animals simultaneously with vitamins and minerals in bolus or single capsule formulations, the microorganisms often are rendered nonviable” (Col. 6, lines 23-30). Other advantages of the capsule include consolidation of multi-step therapies into easily administered, single-step therapies and ensuring the delivery of correct unit doses (Col. 6, lines 30-36).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a capsule with at least two separate chambers and where different chambers of the capsule contain different materials, in different physical forms, as suggested by Nowak, combine it with the capsule with separate chambers in the form of a capsule-in-capsule (where the top member of the capsule is locked with the

bottom member of the capsule), as suggested by Zimmer, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because the capsule-in-capsule form taught by Zimmer has the advantages of including incompatible substances “such as nutrient supplements and bacteria" in the separate compartments (Col. 1, lines 8-9). Zimmer teaches that the double capsule “includes live cultures of rumen bacteria in a first capsule which is enclosed with vitamin and mineral supplements in a second capsule” (Col. 3, lines 15-17). Moreover, the top member of the capsule is locked with the bottom member of the capsule to seal the components of the capsule.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of a multi-compartment capsule would have been obvious over the capsule with at least two separate chambers taught by Nowak. The limitation of a first receiving chamber that comprises at least one ingredient having a first physical state and a second receiving chamber that comprises at least one ingredient having a second physical state would have been obvious over the capsule that contains different materials (Page 2) and that is used to deliver two separate pharmaceutical preparations (Page 3), as taught by Nowak. The limitation of the first

physical state of the ingredient in the first receiving chamber being different from the second physical state of the ingredient in the second receiving chamber would have been obvious over the different materials with different physical forms (liquid and solid) taught by Nowak (Page 2). The limitation of the ingredient in the first receiving chamber being different from the ingredient of the second receiving chamber would have been obvious over the encapsulation of different materials (Page 2) and separate pharmaceutical preparations (Page 3) and by the dextromethorphan liquid in one chamber and chlorpheniramine powder in the second chamber of the capsule (Page 10, Example 6), as taught by Nowak.

Regarding instant claims 2 and 38, the limitation of the multi-compartment capsule further comprising a base and a corresponding cap, where the cap is configured to provide a sealing relationship when engaging the base would have been obvious to one skilled in the art over the capsule-in-capsule (where the top member of the capsule is locked with the bottom member of the capsule), as taught by Zimmer (Col. 5, lines 3-6). One with ordinary skill in the art would know that when the top member of the capsule is locked with the bottom member of the capsule, the capsule is effectively sealed.

Regarding instant claims 5 and 45, the limitation of the physical state of the ingredient in the first receiving chamber would have been obvious over the materials with different physical forms (liquid and solid), as taught by Nowak (Page 2).

Regarding instant claims 6 and 46, the limitation of the solid would have been obvious over the inclusion of a smaller delivery capsule (Page 2), and the encapsulation

of a powdered or particulate material in chamber 18 of Figure 1 (Page 8), as taught by Nowak.

Regarding instant claims 7 and 47, the limitation of the liquid would have been obvious over the inclusion of liquids within discrete chambers of the capsule (Page 7) and the dextromethorphan liquid (i.e. a solution of dextromethorphan) in chamber 20 of the capsule (Page 10), as taught by Nowak.

Regarding instant claims 8 and 48, the limitation of a dispersion would have been obvious over the different physical forms, e.g. liquid, solid (e.g. tablet, particulate, powdered), slurry etc., taught by Nowak (Page 2). One with ordinary skill in the art would consider a dispersion, such as the slurry described by Nowak, an obvious example of a dispersion.

Regarding instant claims 9 and 50, the limitation of a third receiving chamber comprising at least one ingredient would have been obvious over the capsule with at least two separate chambers, as taught by Nowak (Page 2). One with ordinary skill in the art would include extra chambers in the capsule since Nowak teaches “at least” two separate chambers. It would be obvious to one with ordinary skill in the art to modify the number of chambers in the capsule depending on the desired number of ingredients that could be incorporated in the separate chambers. The limitation of the ingredient in the third chamber selected from the group consisting of a nutraceutical, a vitamin, a dietary supplement and a mineral would have been obvious over the encapsulation of a wide range of pharmaceutical, culinary, cosmetic etc. ingredients, as taught by Nowak

(Page 6) and over the vitamins and minerals in the second component of the capsule, as taught by Zimmer (Col. 5, lines 40-45).

Regarding instant claim 36, the limitation of a multi-compartment capsule would have been obvious over the capsule with at least two separate chambers taught by Nowak. The limitation of a first receiving chamber that comprises at least one active ingredient having a first physical state and a second receiving chamber that comprises at least one active ingredient having a second physical state would have been obvious over the capsule that contains different materials (Page 2) and that is used to deliver two separate pharmaceutical preparations (Page 3), as taught by Nowak. The limitation of the first physical state of the ingredient in the first receiving chamber being different from the second physical state of the ingredient in the second receiving chamber would have been obvious over the different materials with different physical forms (liquid and solid) taught by Nowak (Page 2). The limitation of the active ingredient in the first receiving chamber being different from the active ingredient of the second receiving chamber and not present in the second receiving chamber would have been obvious over the encapsulation of different materials (Page 2) and separate pharmaceutical preparations (Page 3) and by the dextromethorphan liquid in one chamber and chlorpheniramine powder in the second chamber of the capsule (Page 10, Example 6), as taught by Nowak.

Regarding instant claim 41, the limitation of the ingredient in the first receiving chamber would have been obvious over the encapsulation of a wide range of pharmaceutical, culinary, cosmetic etc. ingredients and the inclusion of the

pharmaceutical active ingredients dextromethorphan and chlorpheniramine in the capsule (Page 10, Example 6 and Page 6), as taught by Nowak.

Regarding instant claim 42, the limitation of the ingredient in the second receiving chamber would have been obvious over the encapsulation of a wide range of pharmaceutical, culinary, cosmetic etc. ingredients and the inclusion of the pharmaceutical active ingredients dextromethorphan and chlorpheniramine in the capsule (Page 10, Example 6 and Page 6), as taught by Nowak.

Regarding instant claims 43 and 127, the limitation of the ingredient in the first receiving chamber being a pharmaceutical and the ingredient in the second receiving chamber being a pharmaceutical would have been obvious over the encapsulation of the pharmaceutical active ingredients dextromethorphan and chlorpheniramine in the capsule (Page 10, Example 6 and Page 6), as taught by Nowak.

Regarding instant claim 44, the limitation of a pharmaceutical as the ingredient in the first receiving chamber and a biotechnical, a nutraceutical, a vitamin, a dietary supplement or a mineral as the ingredient in the second receiving chamber would have been obvious over the encapsulation of different materials (Page 2) and separate pharmaceutical preparations (Page 3) as taught by Nowak in view of the vitamins and minerals in the second component of the capsule, as taught by Zimmer (Col. 5, lines 40-45). One with ordinary skill in the art would choose different materials for the components of the capsule based on the desired therapeutic effect. Given the teachings of Nowak and Zimmer, one with ordinary skill in the art would modify the components of the first and second chamber to include a pharmaceutical ingredient in one chamber

and a nutraceutical, vitamin, dietary supplement or mineral in the other chamber during the process of routine experimentation.

Regarding instant claim 49, the limitation of at least one of the receiving chambers comprising a time-release coating would have been obvious over the "coatings such as ethyl cellulose (that) can be used to retard solubility times, as taught by Nowak (Page 4). Nowak also teaches, "A further example is use of expanded HPMC defining one compartment and non- expanded HPMC defining another compartment. Expanded HPMC film releases rapidly in the mouth while standard, non-expanded film has sufficient resistance to dissolution to release only after it has been swallowed, providing that it is not kept in the mouth too long" (Page 4).

Regarding instant claims 51-53, the limitation of the ingredient in the third chamber selected from the group consisting of a pharmaceutical, a biotechnical, a nutraceutical, a vitamin, a dietary supplement and a mineral would have been obvious over the encapsulation of a wide range of pharmaceutical, culinary, cosmetic etc. ingredients, as taught by Nowak (Page 6) and over the vitamins and minerals in the second component of the capsule, as taught by Zimmer (Col. 5, lines 40-45). One with ordinary skill in the art would choose different materials for the components of the capsule based on the desired therapeutic effect. Given the teachings of Nowak and Zimmer, one with ordinary skill in the art would add different components to the first, second, and third chambers (selected from pharmaceutical, biotechnical, nutraceutical, vitamin, dietary supplement or mineral) during the process of routine experimentation. Regarding instant claim 52, the limitation of the ingredient in the third receiving chamber

being different from the ingredients in the first and second receiving chamber would have been obvious because one with ordinary skill in the art would incorporate a different ingredient in the third chamber to reduce multiple dosing and effectively deliver more than two ingredients in one capsule. Regarding instant claim 53, the limitation of the ingredient in the third receiving chamber being at a different physical state from the ingredients in the first and second receiving chamber would have been obvious because Nowak teaches a plurality of ingredient phases in different compartments of the capsule. One with ordinary skill in the art would incorporate an ingredient with a different physical state in the third chamber to reduce the need for separate dosing of an ingredient with a physical state different from the other two ingredients.

Regarding instant claims 106-118, 121, and 128, the combination of liquid vitamin E with solid active ingredients glucosamine/chondroitin, S-adenosylmethionine (SAMe), curcumin, Holy Basil, Zinc, Vitamin C, Fluoxetine, Rofecoxib, Diphenhydramine HCl, and Celecoxib along with the liquid omega-3 fatty acids DHA and EPA would have been obvious to one skilled in the art over the different physical forms (liquid and solid) in different chambers of the capsule, as taught by Nowak (Page 2). One skilled in the art would use solid active ingredients and liquid active ingredients (liquid Vitamin E and liquid omega-3 fatty acids DHA and EPA) in the multi-compartment capsule to enhance the therapeutic effectiveness and reduce the need for using separate capsules for ingredients with different physical states.

Regarding instant claim 122, the limitation of the ingredient of the first receiving chamber being a first non-excipient ingredient and the ingredient of the second

receiving chamber being a second non-excipient ingredient, and where the first non-excipient ingredient is different from the second non-excipient ingredient and not present in the second receiving chamber would have been obvious over the encapsulation of the non-excipient ingredient dextromethorphan in the first chamber and the non-excipient ingredient chlorpheniramine in the second chamber of the capsule (Page 10, Example 6 and Page 6), as taught by Nowak.

Regarding instant claims 137-140, the limitation of the ingredient of the first receiving chamber being incompatible (pharmaceutically incompatible) with the ingredient of the second receiving chamber would have been obvious over the encapsulation of materials that are desirably kept separate prior to delivery, as taught by Nowak (Page 6) and the capsule that preserves the activity of mutually reactive or otherwise incompatible substances by physically separating them during production, storage and administration, as taught by Zimmer (Col. 6, lines 23-30).

Regarding instant claims 141-142, the limitation of the hard shell capsule would have been obvious over the suggestion of hard shell gelatin capsules for the delivery of mutually reactive or otherwise incompatible substances (Col. 2, lines 45-56). While discussing the background prior art Zimmer states that it is unlikely that Morishita's (US 4,695,466) soft outer capsules will be able to withstand common shipping, storage and administration conditions.

Regarding instant claims 143-144, the limitations of the multi-compartment capsule that provides for the stability and sufficient shelf-life of the ingredients to make the multi-compartment capsule fit for human consumption would have been obvious

over the example taught by Nowak regarding the co-administering of Accutane and birth control drugs to fertile female users (Pages 3-4).

11. Claims 3-4, 37 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nowak et al. (WO 01/03676) in view of Zimmer (US 5,310,555) and further in view of Rashid et al. (US 5,750,143).

The teachings of Nowak and Zimmer with respect to a multi-compartment capsule and a base and a cap (respectively) are stated above.

Nowak and Zimmer do not expressly teach a cap comprising a configuration to reduce dead volume space within the first receiving chamber.

Rashid teaches a controlled release capsule where "although conventionally shaped round caps may be used, the cap is preferably substantially flattened compared to conventional caps so as to accommodate a tablet whilst retaining the compact nature of the capsule by minimising dead space in the first volume" (Col. 2, lines 63-67).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a capsule with at least two separate chambers and where different chambers of the capsule contain different materials, in different physical forms, as suggested by Nowak, combine it with the capsule with separate chambers in the form of a capsule-in-capsule (where the top member of the capsule is locked with the bottom member of the capsule), as suggested by Zimmer, further combine it with reducing the dead volume space by using a cap with a different configuration, as suggested by Rashid, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do reduce the dead volume space in capsules in order to minimize oxidation and to maximize the dosing efficiency of each capsule.

Regarding instant claims 3-4, 37 and 39, the limitation of the cap comprising a configuration adapted to reducing the dead volume space within the first receiving chamber would have been obvious over reducing the dead volume space by using a cap with a different configuration, as taught by Rashid (Col. 2, lines 63-67).

12. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nowak et al. (WO 01/03676) in view of Zimmer (US 5,310,555) and further in view of Story (US 5,738,871).

The teachings of Nowak and Zimmer with respect to a multi-compartment capsule and a base and a cap (respectively) are stated above.

Nowak and Zimmer do not expressly teach a filling material to reduce dead volume space within the first receiving chamber.

Story teaches hard gelatin capsules containing a fat-soluble nutrient, a nonionic surfactant, a gelatin softening agent and optionally water (Col. 2, lines 47-50). “In cases of small quantities of active … it is not actually necessary to have so much surfactant, but it is left in for convenience in filling and so as to not have so much dead space in the capsule” (Col. 6, lines 23-27).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a capsule with at least two separate chambers and where

different chambers of the capsule contain different materials, in different physical forms, as suggested by Nowak, combine it with the capsule with separate chambers in the form of a capsule-in-capsule (where the top member of the capsule is locked with the bottom member of the capsule), as suggested by Zimmer, further combine it with reducing the dead volume space by using filling material such as surfactants, as suggested by Story, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do reduce the dead volume space in capsules in order to minimize oxidation and to maximize the dosing efficiency of each capsule.

Regarding instant claim 40, the limitation of a filling material introduced into the cap to reduce the dead volume space within the first receiving chamber would have been obvious over the use of filling material such as surfactants to reduce the dead volume space, as taught by Story.

Conclusion

13. Due to the new grounds of rejection, this action is made non-final.

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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